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PATENT  
A-72018  
Attorney Docket No.: 014643-012110US  
Serial No. 10/000,433

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

*In re* application of:

TOMIZUKA et al.

Serial No. 10/000,433

Filing Date: November 30, 2001

For: *Transgenic Transchromosomal  
Rodents for Making Human  
Antibodies*

Examiner: LI, Q. Janice

Group Art Unit: 1632

CERTIFICATE OF MAILING

I hereby certify that this correspondence, including listed enclosures, is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450:

Dated: May 6, 2003

Signed: Jere Valles

Jere Valles

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Sir:

In satisfaction of the duty of disclosure under 37 C.F.R. § 1.56, and in accordance with the provisions of 37 C.F.R. §§ 1.97 and 1.98, Applicants wish to draw the attention of the U.S. Patent and Trademark Office to the references cited on the accompanying form PTO/SB/8A.

Copies of the references are enclosed.

Further, in accordance with the provisions of 37 C.F.R. §§ 1.97(c) and 1.97(e)(1), the undersigned certifies that references A13, C87, and C94, listed on the enclosed form PTO/SB/8A, were first cited in the International Search Report dated February 6, 2003, for a counterpart PCT application. As such, the filing of the instant Information Disclosure Statement is within three months of the date of that International Search Report and, therefore, need not be

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accompanied by the fee as set forth in 37 C.F.R. § 1.17(p). A copy of the International Search Report for the counterpart PCT application is enclosed herewith.

None of the foregoing references are believed to disclose the invention as claimed.

Nothing herein shall constitute an admission concerning the contents of any of the cited references, nor shall the inclusion of a reference herein be considered an admission that the reference constitutes prior art against the invention claimed in the above-identified application. Submission of the present document shall not be construed as an admission that a search has been made or that better art does not exist.

As far as is known to the undersigned, this Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits as set forth in 37 C.F.R. § 1.97(b), and therefore no fee is required. Although no fee is believed to be due, the Commissioner is authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-2319 (Our Order No. 455675-00083 (A-72018/GKS/THR)).

Respectfully submitted,  
DORSEY & WHITNEY LLP

Dated: 06 May 2003  
Dorsey & Whitney LLP  
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*Customer Number: 32940*

Attachments : Form PTO/SB/8A  
Copies of references cited on Form PTO/SB/8A  
International Search Report for PCT/US01/45293



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Substitute for form 1449A/PTO  
(Modified)

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	7	Attorney Docket Number	014643-012110US (A-72018/455675-83)
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### Complete if Known

Application Number	10/000,433
Filing Date	November 30, 2001
First Named Inventor	TOMIZUKA, Kazuma
Group Art Unit	
Examiner Name	

### U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	U.S. Patent Document Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	A1	5,175,384	12-1992	Krimpenfort	
	A2	5,204,244	04-1993	Fell et al.	
	A3	5,416,260	05-1995	Jikker	
	A4	5,434,340	07-1995	Krimpenfort	
	A5	5,545,806	08-1996	Lonberg et al.	
	A6	5,545,807	08-1996	Surani	
	A7	5,569,825	10-1996	Lonberg et al.	
	A8	5,625,126	04-1997	Lonberg et al.	
	A9	5,633,425	05-1997	Lonberg et al	
	A10	5,661,016	08-1997	Lonberg et al	
	A11	5,698,196	12-1997	Matsushima	
	A12	5,702,946	12-1997	Doerschuk	0007/09/01 2002
	A13	5,770,429	06-1998	Lonberg et al.	
	A14	5,789,650	08-1998	Lonberg et al.	
	A15	5,814,318	09-1998	Lonberg et al.	
	A16	5,939,598	08-1999	Kucherlapati et al.	
	A17	5,874,299	02-1999	Lonberg et al.	
	A18	5,877,397	03-1999	Lonberg et al.	
	A19	6,300,129	10-2001	Lonberg et al	

### FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>2</sup> Number <sup>4</sup> Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
	B1	EP 0 315 062 ✓	05-1989			
	B2	WO 90/04036 ✓	04-1990			
	B3	WO 90/12878 ✓	11-1990			
	B4	WO 91/00906 ✓	01-1991			
	B5	WO 91/10741 ✓	07-1991			
	B6	WO 92/03918 ✓	03-1992			
	B7	WO 96/02576 ✓	02-1996			

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**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

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✓	C59	NUSSENZWEIG, M.C., et al., "A human immunoglobulin gene reduces the incidence of lymphomas in c-Myc-bearing transgenic mice", <i>Nature</i> 336:446-450 (1988).	
✓	C60	OETTINGER, M.A., et al., "RAG-1 and RAG-2, Adjacent Genes That Synergistically Activate V(D)J Recombination", <i>Science</i> 248:1517-1523 (1990).	
✓	C61	PETTERS, R.M., "Transgenic mice in immunological research", <i>Vet. Immunol. Immunopath.</i> 17:267-278 (1987).	
✓	C62	PETTERSSON, S., et al., "A second B cell-specific enhancer 3' of the immunoglobulin heavy-chain locus", <i>Nature</i> 344:165-168 (1990).	
✓	C63	RABBİTTS, T.H., et. al., "Human immunoglobulin heavy chain genes: evolutionary comparisons of C $\mu$ , C $\delta$ and C $\gamma$ genes and associated switch sequences", <i>Nucl. Acids Res.</i> 9:4509-4524 (1981).	
✓	C64	RATH, S., et al., "B cell abnormalities induced by a $\mu$ Ig transgene extend to L chain isotype usage", <i>J. of Immunol.</i> 146:2841 (1991).	
✓	C65	RATH, S., et al., "Quantitative analysis of idiotypic mimicry and allelic exclusion in mice with a $\mu$ Ig Transgene", <i>J. of Immunol.</i> 143:2074-2080 (1989).	
✓	C66	RAVETCH, J.V., et al., "Evolutionary approach to the question of immunoglobulin heavy chain switching: Evidence from cloned human and mouse genes", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 77:6734-6738 (1980).	
✓	C67	REID, L.E., et al., "A single DNA response element can confer inducibility by both $\alpha$ - and $\gamma$ -interferons", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 86:840-844 (1989).	
✓	C68	RITCHIE, K.A., et al., "Allelic exclusion and control of endogenous immunoglobulin gene rearrangement in $\kappa$ transgenic mice", <i>Nature</i> 312:517-520 (1984).	
✓	C69	ROTHMAN, P., et al., "Structure and expression of germline immunoglobulin $\gamma$ 3 heavy chain gene transcripts: implications for mitogen and lymphokine directed class-switching", <i>Intl. Immunol.</i> 2:621-627 (1990).	
✓	C70	RUSCONI, S., et al., "Transmission and expression of a specific pair of rearranged immunoglobulin $\mu$ and $\kappa$ genes in a transgenic mouse line", <i>Nature</i> 314:330-334 (1985).	
✓	C71	SATO, T., et al., "Physical linkage of a variable region segment and the joining region segment of the human immunoglobulin heavy chain locus", <i>Biochem. Biophys. Res. Comm.</i> 154:264-271 (1988).	
✓	C72	SCANGOS, G., and BIEBERICH, C., "Gene transfer into mice", <i>Advances in Genetics</i> 24: 285-322 (1987).	
✓	C73	SEVIDY, J.M., and SHARP, P.A., "Positive genetic selection for gene disruption in mammalian cells by homologous recombination", <i>Proc. Natl. Acad. Sci. USA</i> 86:227-231 (1989).	
	C74	SHIMIZU, A., et al., "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse", <i>Proc. Natl. Acad. Sci. USA</i> 86:8020-8023 (1989).	
✓	C75	SHIMIZU, A., et al., "Trans-Splicing as a Possible Molecular Mechanism for the Multiple Isotype Expression of the Immunoglobulin Gene", <i>J. Exp. Med.</i> 173:1385-1393 (1991).	
✓	C76	SHIN, E. K., et al., "Physical Map of the 3' Region of the Human Immunoglobulin Heavy Chain Locus: Clustering of Autoantibody-reacted Variable Segments in One Haplotype", <i>The EMBO J.</i> : 10, 3641-3645 (1991).	
	C77	SIDERAS, P., et al., "Production of sterile transcripts by C $\gamma$ genes in an IgM-producing human neoplastic B cell line that switches to IgG-producing cells", <i>Intl. Immunol.</i> 1: 631-642 (1989).	
	C78	SIEBENLIST, U., et al., "Human immunoglobulin D segments encoded in tandem multigenic families", <i>Nature</i> 294:631-635 (1981).	

Examiner Signature	Date Considered
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Substitute for form 1449A/PTO (Modified)				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/000,433
(use as many sheets as necessary)				Filing Date	November 30, 2001
Sheet	4	of	7	First Named Inventor	TOMIZUKA, Kazuma
				Group Art Unit	TECH CENTER 1600/2900
				Examiner Name	
				Attorney Docket Number	014643-012110US (A-72018/455675-83)

### OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>6</sup>
✓	C39	KOLLER, B.H., and SMITHIES, O., "Inactivating the $\beta_2$ -microglobulin locus in mouse embryonic stem cells by homologous recombination", <i>Proc. Natl. Acad. Sci. USA</i> 86:8932-8935 (1989).	
✓	C40	LIN, F.L., et al., "Recombination in mouse L cells between DNA introduced into cells and homologous chromosomal sequences", <i>Proc. Natl. Acad. Sci. USA</i> 82:1391-1395 (1985).	
✓	C41	LINTON, P.-J., et al., "Primary Antibody-Forming Cells and Secondary B Cells Are Generated from Separate Precursor Cell Subpopulations", <i>Cell</i> 59:1049-1059 (1989).	
✓	C42	LO, D., et al., "Expression of mouse IgA by transgenic mice, pigs and sheep", <i>Eur. J. Immunol.</i> 21:1001-1006 (1991).	
✓	C43	LONBERG, M., et al., "Antigen-specific human antibodies from mice comprising four distinct genetic modifications", <i>Nature</i> 368:856-859 (1994).	
✓	C44	LORENZ, W., et al., "Physical map of the human immunoglobulin $\lambda$ locus and its implications for the mechanisms of $V_{\kappa}$ - $J_{\kappa}$ rearrangement", <i>Nucl. Acids Res.</i> 15:9667-9676 (1987).	
✓	C45	LUTZKER, S., and ALT, F.W., "Structure and Expression of Germ Line Immunoglobulin $\gamma 2b$ Transcripts", <i>Mol. Cell Biol.</i> 8:1849-1852 (1988).	
✓	C46	MANSOUR, S.L., et al., "Disruption of the proto-oncogene <i>int-2</i> in mouse embryo-derived stem cells: a general strategy for targeting mutations to non-selectable genes", <i>Nature</i> 336:348-352 (1988).	
✓	C47	MILLER, J., et al., "Structural alterations in J regions of mouse immunoglobulin $\lambda$ genes are associated with differential gene expression", <i>Nature</i> 295:428-430 (1982).	
✓	C48	MILLS, F.C., et al., "DNase I hypersensitive sites in the chromatin of human $\mu$ immunoglobulin heavy-chain genes", <i>Nature</i> 306:809-812 (1983).	
✓	C49	MILLS, F.C., et al., "Sequences of human immunoglobulin switch regions: implications for recombination and transcription", <i>Nucl. Acids. Res.</i> 18:7305-7316 (1991).	
✓	C50	MORRISON, S.L., "Success in specification", <i>Nature</i> 368:812-813 (1994).	
✓	C51	MOWATT, M.R., et al., "DNA sequence of the murine $\gamma 1$ switch segment reveals novel structural elements", <i>J. Immunol.</i> 136:2674-2683 (1986).	
✓	C52	MÜLLER, W., et al., "Membrane-bound IgM obstructs B cell development in transgenic mice", <i>Eur. J. Immunol.</i> 19:923-928 (1989).	
✓	C53	MURRAY, A.W., and SZOSTAK, J.W., "Construction of artificial chromosomes in yeast", <i>Nature</i> 305:189-193 (1983).	
✓	C54	NIKAIKO, T., et al., "Nucleotide Sequences of Switch Regions of Immunoglobulin C and C Genes and Their Comparison", <i>J. Biol. Chem.</i> 257:7322-7329 (1982).	
✓	C55	NIKAIKO, T., et al., "Switch region of immunoglobulin C $\mu$ gene is composed of simple tandem repetitive sequences", <i>Nature</i> 292:845-848 (1981).	
✓	C56	NEUBERGER, M.S., et al., "Isotype exclusion and transgene down-regulation in immunoglobulin- $\lambda$ transgenic mice", <i>Nature</i> 338:350-352 (1989).	
✓	C57	NEUBERGER, M.S., "Generating high-avidity human Mabs in mice", <i>Nature Biotechnology</i> 14:826 (1996).	
✓	C58	NUSSENZWEIG, M.C., et al., "Allelic exclusion in transgenic mice carrying mutant human IgM genes", <i>J. Exp. Med.</i> 167:1969 (1988).	

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Sheet	3	of	7	Application Number	10/000,433
				Filing Date	November 30, 2001
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<b>OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
✓	C20	FISHWILD, D.M., et al. "High-Avidity human IgG $\kappa$ monoclonal antibodies from a novel strain of minilocus transgenic mice", <i>Nature Biotechnology</i> 14:845. (1996).			
✓	C21	FORNI, L., "Extensive splenic B cell activation in IgM-transgenic mice", <i>Eur. J. Immunol.</i> 20:983-989 (1990).			
✓	C22	GERSTEIN, R.M., et al., "Isotype Switching of an Immunoglobulin Heavy Chain Transgene Occurs by DNA Recombination between Different Chromosomes", <i>Cell</i> 63:537-548 (1990).			
✓	C23	GOODHARDT, M., et al., "Rearrangement and expression of rabbit immunoglobulin $\kappa$ light chain gene in transgenic mice", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 84:4229-4233 (1987).			
	C24	GORDON, J., "Transgenic mice in immunology", <i>The Mount Sinai Journal of Medicine</i> , 53:223-231 (1986).			
✓	C25	GREEN, L.L., et al., "Antigen-specific human monoclonal antibodies from mice engineered with human Ig heavy and light chain YACs", <i>Nature Genetics</i> 7:13-21 (1994).			
✓	C26	HAGMAN, J., et al., "Inhibition of immunoglobulin gene rearrangement by the expression of a $\lambda 2$ transgene", <i>J. Exp. Med.</i> 169:1911-1929 (1989).			
✓	C27	HOFKER, M.H., et al., "Complete physical map of the human immunoglobulin heavy chain constant region gene complex", <i>Proc. Natl. Acad. Sci. USA</i> 86:5567-5571 (1989).			
✓	C28	HUMPHRIES, C.G., et al., "A new human immunoglobulin V <sub>H</sub> family preferentially rearranged in immature B-cell tumours", <i>Nature</i> 331:446-449 (1988).			
✓	C29	HUXLEY, C., et al., "The human HPRT gene on a yeast artificial chromosome is functional when transferred to mouse cells by cell fusion." <i>Genomics</i> 1991 Apr;9(4):742-50.			
✓	C30	ICHIHARA, Y., et al., "Organization of human immunoglobulin heavy chain diversity gene loci", <i>The EMBO J.</i> 7:4141-4150 (1988).			
✓	C31	IGLESIAS, A., et al., "Expression of immunoglobulin delta chain causes allelic exclusion in transgenic mice", <i>Nature</i> 330:482-484 (1987).			
✓	C32	JAENISCH, R., "Transgenic Animals", <i>Science</i> 240:1468-1474 (1988).			
	C33	JAKOBOVITS, A., et al., "Analysis of homozygous mutant chimeric mice: Deletion of the immunoglobulin heavy-chain joining region blocks B-cell development and antibody production", <i>Proc. Natl. Acad. Sci. USA</i> 90:2551-2555 (1993).			
✓	C34	JAMES, K., and BELL, G.T., "Human monoclonal antibody production current status and future prospects", <i>J. of Immunol. Methods</i> 100:5-40 (1987).			
✓	C35	JASIN, M., and BERG, P., "Homologous integration in mammalian cells without target gene selection", <i>Genes &amp; Development</i> 2:1353-1363 (1988).			
✓	C36	JUNG, S., et al., "Shutdown of Class Switching Recombination by Deletion of a Switch Region Control Element", <i>Science</i> 259:984-987 (1993).			
✓	C37	KENNY, J.J., et al., "Alteration of the B cell surface phenotype, immune response to phosphocholine and the B cell repertoire in M167 $\mu$ plus $\kappa$ transgenic mice", <i>J. of Immunol.</i> 142:4466-4474 (1989).			
✓	C38	KITAMURA, D., et al., "A B cell-deficient mouse by targeted disruption of the membrane exon of the immunoglobulin $\mu$ chain gene", <i>Nature</i> 350:423-426 (1991).			

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✓	C1	ALT, F.W., et al., "Immunoglobulin genes in transgenic mice", <i>Trends in Genetics</i> , 231-236, (Aug. 1985).	
✓	C2	BERMAN, J.E., et. al., "Content and organization of the human Ig V <sub>H</sub> locus: definition of three new V <sub>H</sub> families and linkage to the Ig C <sub>H</sub> locus", <i>The EMBO J.</i> 7:727-738 (1988).	
✓	C3	BERTON, M.T., et. al., "Synthesis of germ-line $\gamma$ 1 immunoglobulin heavy-chain transcripts in resting B cells: Induction by interleukin 4 and inhibition by interferon $\gamma$ ", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 86:2829-2833 (1989).	
✓	C4	BOLLAG, R.J., et al., "Homologous recombination in mammalian cells", <i>Annu. Rev. Genet.</i> 23:199-225 (1989).	
✓	C5	BRUGGEMANN, M., et al., "A repertoire of monoclonal antibodies with human heavy chains from transgenic mice", <i>Proc. Natl. Acad. Sci. USA</i> 86:6709-6713 (1989).	
✓	C6	BRUGGEMANN, M., et al., "Human antibody production in transgenic mice: expression from 100 kb of the human IgH locus", <i>Eur. J. Immunol.</i> 21:1323-1326 (1991).	
✓	C7	BUCCININI, D., et al., "Rearrangement of a chicken immunoglobulin gene occurs in the lymphoid lineage of transgenic mice", <i>Nature</i> 326:409-411 (1987).	
✓	C8	BUTTIN, G., "Exogenous Ig gene rearrangement in transgenic mice: a new strategy for human monoclonal antibody production?" <i>Trends in Genetics</i> --vol. 3, No. 8, 205-206 (Aug. 1987).	
✓	C9	CAPECCHI, M.R., "Altering the genome by homologous recombination", <i>Science</i> 244:1288-1292 (1989).	
✓	C10	CAPECCHI, M.R., "The new mouse genetics: Altering the genome by gene targeting", <i>Trends in Genetics</i> 5:70-76 (1989).	
✓	C11	CHOI, T.K., et al., "Transgenic mice containing a human heavy chain immunoglobulin gene fragment cloned in a yeast artificial chromosome." <i>Nat Genet.</i> 1993 Jun;4(2):117-23.	
✓	C12	COFFMAN, R.L., et al., "A mouse T cell product that preferentially enhances IgA production", <i>J. Immunol.</i> 139:3685-3690 (1987).	
✓	C13	COFFMAN, R.L., and CARTY, J. "A T cell activity that enhances polyclonal IgE production and its inhibition by interferon- $\gamma$ ", <i>J. Immunol.</i> 136:949-954 (1986).	
✓	C14	DAVIES, N.P., et al., "Creation of Mice Expressing Human Antibody Light Chains by Introduction of a Yeast Artificial Chromosome Containing the Core Region of the Human Immunoglobulin $\kappa$ Locus." <i>Biotechnology (N Y)</i> . 1993 Aug;11(8):911-4.	
✓	C15	DAVIES, N.P., et al., "Targeted Alterations in Yeast Artificial Chromosomes for Inter-Species Gene Transfer", <i>Nucleic Acid Res.</i> 20: 2693-2698 (1992).	
✓	C16	DOETSCHMAN, T., et al., "Targeted correction of a mutant HPRT gene in mouse embryonic stem cells", <i>Nature</i> 330:576-578 (1987).	
✓	C17	DURDIK, J., et al., "Isotype switching by a microinjected $\mu$ immunoglobulin heavy chain gene in transgenic mice", <i>Proc. Natl. Acad. Sci. USA</i> 86:2346-2350 (1989).	
✓	C18	ESSER, C., and RADBRUCH, A., "Rapid induction of transcription of unarranged S $\gamma$ 1 switch regions in activated murine B cells by interleukin 4", <i>The EMBO J.</i> 8:483-488 (1989).	
✓	C19	FERRIER, P., et al., "Separate elements control DJ and VDJ rearrangement in a transgenic recombination substrate", <i>The EMBO J.</i> 9:117-125 (1990).	

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### Complete if Known

Application Number	10/000,433
Filing Date	November 30, 2001
First Named Inventor	TOMIZUKA, Kazuma
Group Art Unit	
Examiner Name	

### OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
✓	C79	SMITHIES, O., et al., "Insertion of DNA sequences into the human chromosomal $\beta$ -globin locus by homologous recombination", <i>Nature</i> 317:230-234 (1985).
✓	C80	SNAPPER, C.M., and Paul, W.E., "Interferon- $\gamma$ and B Cell Stimulatory Factor-1 Reciprocally Regulate Ig Isotype Production", <i>Science</i> 236:944-947 (1987).
✓	C81	SONG, K.-Y., et al., "Accurate modification of a chromosomal plasmid by homologous recombination in human cells", <i>Proc. Natl. Acad. Sci. USA</i> 84:6820-6824 (1987).
✓	C82	STAVNEZER, J., et al., "Immunoglobulin heavy-chain switching may be directed by prior induction of transcripts from constant-region genes", <i>Proc. Natl. Acad. Sci. (U.S.A.)</i> 85:7704-7708 (1988).
✓	C83	STORB, U., et al., "Expression, Allelic Exclusion and Somatic Mutation of Mouse Immunoglobulin Kappa Genes", <i>Immunological Reviews</i> 89:85-102 (1986).
✓	C84	STORB, U., "Immunoglobulin Gene Analysis in Transgenic Mice, in <i>Immunoglobulin Genes</i> , Academic Press Limited, pp. 303-326 (1989).
✓	C85	SZUREK, P., et al., "Complete nucleotide sequence of the murine $\gamma$ 3 switch region and analysis of switch recombination in two $\gamma$ 3-expressing hybridomas", <i>J. Immunol.</i> 135:620-626 (1985).
✓	C86	TAHARA, T., et al., "HLA antibody responses in HLA class I transgenic mice", <i>Immunogenetics</i> 32:351-360 (1990).
✓	C87	TAKAI, T., et al., "Augmented Humoral and Anaphylactic Responses in Fc $\gamma$ RII-deficient Mice", <i>Nature</i> 379:346-349 (1996).
✓	C88	TAKI, S., et al., "Targeted Insertion of a Variable Region Gene into the Immunoglobulin Heavy Chain Locus", <i>Science</i> 262:1268-1271 (1993).
✓	C89	TANAKA, T., et al., "An Antisense Oligonucleotide Complementary to a Sequence in $\gamma$ 2b Increase $\gamma$ 2b Germline Transcripts, Stimulates B cell DNA Synthesis, and Inhibits Immunoglobulin Secretion", <i>The Journal of Experimental Medicine</i> 175:597-607 (1992).
	C90	TAUSSIG, M.J., et al., "Regulation of immunoglobulin gene rearrangement and expression", <i>Immunology Today</i> 10:143-146 (1989).
✓	C91	TAYLOR, L.D., et al., "Human immunoglobulin transgenes undergo rearrangement, somatic mutation and class switching in mice that lack endogenous IgM", <i>International Immunology</i> 6:579-591 (1994).
✓	C92	THOMAS, K.R., and CAPECCHI, M.R., "Site-Directed Mutagenesis by Gene Targeting in Mouse Embryo-Derived Stem Cells", <i>Cell</i> 51:503-512 (1987).
✓	C93	THOMAS, K.R., et al., "High Frequency Targeting of Genes to Specific Sites in the Mammalian Genome", <i>Cell</i> 44:419-428 (1986).
✓	C94	TOMIZUKA, K., et al., "Double Trans-Chromosomal Mice: Maintenance of Two Individual Human Chromosome Fragments Containing Ig Heavy and Kappa Loci and Expression of Fully Human Antibodies," <i>Proc. Nat. Acad. Sci (USA)</i> 97:722-727 (2000).
✓	C95	UHLMANN, E., and PEYMAN, A., "Antisense Oligonucleotides: A new therapeutic principle," <i>Chemical Reviews</i> 90:544-584 (1990).
	C96	VLASOV, et al., "Arrest of immunoglobulin G mRNA translation in vitro with an alkylating antisense oligonucleotide derivative", <i>Chemical Abstracts</i> , p. 28, 112:22943X (1990).
✓	C97	WAGNER, S.D., et al. "Antibodies generated from human immunoglobulin miniloci in transgenic mice." <i>Nucleic Acids Res.</i> 1994 Apr 25;22(8):1389-93.

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✓	C98	WEAVER, D., et al., "A Transgenic Immunoglobulin Mu Gene Prevents Rearrangement of Endogenous Genes", <i>Cell</i> 42:117-127 (1985).	
✓	C99	WEISS, R., "Mice Making Human-Like Antibodies", <i>The Washington Post</i> , Apr. 28, 1994.	
✓	C100	YAMAMURA, K.-I., et al., "Cell-type-specific and regulated expression of a human $\gamma 1$ heavy-chain immunoglobulin gene in transgenic mice", <i>Proc. Natl. Acad. Sci. USA</i> 83:2152-2156 (1986).	
✓	C101	YANCOPOULOS, G.D., and ALT, F.W., "Developmentally Controlled and Tissue-Specific Expression of Unrearranged $V_H$ gene segments", <i>Cell</i> 40:271-281 (1985).	
✓	C102	YANCOPOULOS, G.D., and ALT, F.W., "Regulation of the Assembly and Expression of Variable-Region Genes", <i>Ann. Rev. Immunol.</i> 4:339-368 (1986).	
✓	C103	YASUI, H., et al., "Class switch from $\mu$ to $\delta$ is mediated by homologous recombination between $\sigma_{\mu}$ and $\Sigma_{\mu}$ sequences in human immunoglobulin gene loci", <i>Eur. J. Immunol.</i> 19:1399-1403 (1989).	
✓	C104	ZIJLSTRA, M., et al., "Germ-line transmission of a disrupted $\beta_2$ -microglobulin gene produced by homologous recombination in embryonic stem cells", <i>Nature</i> 342:435-438 (1989).	
✓	C105	ZIMMER, A., and GRUSS, P., "Production of chimaeric mice containing embryonic stem (ES) cells carrying a homoeobox <i>Hox</i> 1.1 allele mutated by homologous recombination", <i>Nature</i> 338:150-153 (1989).	

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